



#7

PATENT

CERTIFICATE OF MAILING

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Jane A. Walker April 3, 2003
Jane A. Walker Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Achilefu et al.
Serial No.: 09/757,332
Filing Date: January 9, 2001
Group Art Unit: 1619
Confirmation No.: 5505
Title: **HYDROPHILIC CYANINE DYES**
Atty Docket No.: MRD-66

Cincinnati, Ohio 45202

April 3, 2003

Box SEQUENCE
P.O. Box 2327
Arlington, VA 22202

STATEMENT UNDER 37 C.F.R. §1.821(e & f)

The substitute paper copy of the "Sequence Listing" submitted herewith for consideration in the above-referenced application and the computer readable copy of that sequence listing submitted herewith are identical.

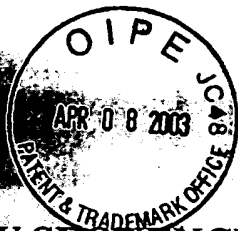
Respectfully submitted,

WOOD, HERRON & EVANS, L.L.P.

Beverly A. Lyman

Beverly A. Lyman, Ph.D.
Reg. No. 41,961

2700 Carew Tower
441 Vine Street
Cincinnati, OH 45202
(513) 241-2324 (voice)
(513) 421-7269 (facsimile)
K:\MRD\66\STATE sequence compliance.wpd



BIOTECHNOLOGY
SYSTEMS
BRANCH



0590
0305

RAW SEQUENCE LISTING **ERROR REPORT**

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: 09/757,332
Source: OIPF
Date Processed by STIC: 2/27/2003

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.

PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:

- 1) INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,**
- 2) TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY**

FOR CRF SUBMISSION QUESTIONS, PLEASE CONTACT MARK SPENCER, 703-308-4212.

FOR SEQUENCE RULES INTERPRETATION, PLEASE CONTACT ROBERT WAX, 703-308-4216.

PATENTIN 2.1 e-mail help: patin21help@uspto.gov or phone 703-306-4119 (R. Wax)

PATENTIN 3.0 e-mail help: patin3help@uspto.gov or phone 703-306-4119 (R. Wax)

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE CHECKER VERSION 3.1 PROGRAM, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:

<http://www.uspto.gov/web/offices/pac/checker>

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.

Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.

Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

- 1. EFS-Bio (<http://www.uspto.gov/ebc/efs/downloads/documents.htm>), EFS Submission User Manual- ePAVE)**
- 2. U.S. Postal Service: U.S. Patent and Trademark Office, Box Sequence, P.O. Box 2327, Arlington, VA 22202**
- 3. Hand Carry directly to:**
U.S. Patent and Trademark Office, Technology Center 1600, Reception Area, 7th Floor, Examiner Name, Sequence Information, Crystal Mall One, 1911 South Clark Street, Arlington, VA 22202
Or
U.S. Patent and Trademark Office, Box Sequence, Customer Window, Lobby, Room 1B03, Crystal Plaza Two, 2011 South Clark Place, Arlington, VA 22202
- 4. Federal Express, United Parcel Service, or other delivery service to: U.S. Patent and Trademark Office, Box Sequence, Room 1B03-Mailroom, Crystal Plaza Two, 2011 South Clark Place, Arlington, VA 22202**

Revised 01/29/2002

Raw Sequence Listing Error Summary

ERROR DETECTED

SUGGESTED CORRECTION

SERIAL NUMBER: 09/757,332

ATTN: NEW RULES CASES: PLEASE DISREGARD ENGLISH "ALPHA" HEADERS, WHICH WERE INSERTED BY PTO SOFTWARE

- 1 Wrapped Nucleics
 Wrapped Aminos The number/text at the end of each line "wrapped" down to the next line. This may occur if your file was retrieved in a word processor after creating it. Please adjust your right margin to 3; this will prevent "wrapping."
- 2 Invalid Line Length The rules require that a line not exceed 72 characters in length. This includes white spaces.
- 3 Misaligned Amino
 Numbering The numbering under each 5th amino acid is misaligned. Do not use tab codes between numbers; use space characters, instead.
- 4 Non-ASCII The submitted file was not saved in ASCII(DOS) text, as required by the Sequence Rules. Please ensure your subsequent submission is saved in ASCII text.
- 5 Variable Length Sequence(s) contain n's or Xaa's representing more than one residue. Per Sequence Rules, each n or Xaa can only represent a single residue. Please present the maximum number of each residue having variable length and indicate in the <220>-<223> section that some may be missing.
- 6 PatentIn 2.0
 "bug" A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid sequences(s) . Normally, PatentIn would automatically generate this section from the previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to the subsequent amino acid sequence. This applies to the mandatory <220>-<223> sections for Artificial or Unknown sequences.
- 7 Skipped Sequences
 (OLD RULES) Sequence(s) missing. If intentional, please insert the following lines for each skipped sequence:
 (2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)
 (i) SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading)
 (xi) SEQUENCE DESCRIPTION:SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)
 This sequence is intentionally skipped

 Please also adjust the "(ii) NUMBER OF SEQUENCES:" response to include the skipped sequences.
- 8 Skipped Sequences
 (NEW RULES) Sequence(s) missing. If intentional, please insert the following lines for each skipped sequence.
 <210> sequence id number
 <400> sequence id number
 000
- 9 Use of n's or Xaa's
 (NEW RULES) Use of n's and/or Xaa's have been detected in the Sequence Listing.
 Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present.
 In <220> to <223> section, please explain location of n or Xaa; and which residue n or Xaa represents.
- 10 Invalid <213>
 Response Per 1.823 of Sequence Rules, the only valid <213> responses are: Unknown, Artificial Sequence, or scientific name (Genus/species). <220>-<223> section is required when <213> response is Unknown or Artificial Sequence
- 11 Use of <220> Sequence(s) 1-8 missing the <220> "Feature" and associated numeric identifiers and responses.
 Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or "Unknown." Please explain source of genetic material in <220> to <223> section.
 (See "Federal Register," 06/01/1998, Vol. 63, No. 104, pp. 29631-32) (Sec. 1.823 of Sequence Rules)
- 12 PatentIn 2.0
 "bug" Please do not use "Copy to Disk" function of PatentIn version 2.0. This causes a corrupted file, resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk.
- 13 Misuse of n n can only be used to represent a single nucleotide in a nucleic acid sequence. N is not used to represent any value not specifically a nucleotide.

delete

SEQUENCE LISTING

delete ALL alphabetical
headers. Use only numeric
identifiers in new sequence header
format

09/957,332 1

delete

<110> APPLICANT: Samuel I. Achilefu
Raghavan Rajagopalan
Richard B. Dorshow
Joseph E. Bugaj
delete ASSIGNEE: Mallinckrodt Inc.

pg 1-3

Does No: Comply
Corrected Diskette Needed

<120> ~~TITLE~~ Hydrophilic Cyanine Dyes

<130> ~~DOCKET/FILE REFERENCE~~: MRD-66

<150> ~~PRIOR APPLICATION NUMBER~~: US 09/484,319

<151> ~~FILING DATE~~: 2000-01-18

<160> ~~NUMBER OF SEQUENCES~~: 8

<170> ~~SOFTWARE~~: FastSEQ for Windows Version 3.0

<210> ~~SEQ ID NO~~: 1

<211> ~~LENGTH~~: 8

<212> ~~TYPE~~: PRT

<213> ~~ORGANISM~~ Synthetic

<220>

MOD_RES

<221> (1) ... delete

<222> delete

<223> Xaa = D-Phe

<224> ~~Xbb~~ = Cys with an intramolecular disulfide bond
Xaa between two Cys amino acids

<225> Xcc = D-Trp

Xaa

<400> ~~SEQ ID NO~~: 1

Xaa Xbb Tyr Xcc Lys Thr Xbb Thr

1 5

These are invalid. Use Xaa at all times

<210> ~~SEQ ID NO~~: 2

<211> ~~LENGTH~~: 8

<212> ~~TYPE~~: PRT

<213> ~~ORGANISM~~ Synthetic

<221> MOD_RES

<222> (1) ..(0) delete

<223> Xaa = D-Phe

<224> ~~Xaa-Xbb~~ = Cys with an intramolecular disulfide bond
between two Cys amino acids

<225> Xaa-Xcc = D-Trp

<226> Xaa-Xdd = Thr-OH

Xaa

<400> ~~SEQ ID NO~~: 2

Xaa Xbb Tyr Xcc Lys Thr Xbb Xdd

1 5

<210> ~~SEQ ID NO~~: 3

<211> ~~LENGTH~~: 11

These
don't exist
per sequence
header

invalid response - see items 10 and 11 on
Even Summary
sheet

insert this mandatory
numeric identifier
wherever <221>, <222>, or
<223> is shown

<221> mod.RES
<222> (2), (7)
<223> ↑
? <221> mod.RES.
<222> (4)
<223> ↑

<220> mandatory

<221> mod.RES
<222> (2), (7)
<223> ↑

<221> mod.RES
<222> (4)
<223> ↑

<221> mod.RES
<222> (8)
<223> ↑

Xaa Xbb Tyr Xcc
1 invalid

09/757,332 2

<212> ~~TYPE: PRT~~
 <213> ~~ORGANISM: Synthetic~~ → <2207>
 <221> MOD_RES
 <222> (1) ~~... (0)~~ delete
 <400> ~~SEQ ID NO: 3~~
 Gly Ser Gly Gln Trp Ala Val Gly His Leu Met
 1 5 10

<210> ~~SEQ ID NO: 4~~
 <211> ~~LENGTH: 11~~
 <212> ~~TYPE: PRT~~
 <213> ~~ORGANISM: Synthetic~~ → <2207>
 <221> MOD_RES
 <222> (1) ~~... (0)~~ delete
 <400> ~~SEQ ID NO: 4~~
 Gly Asp Gly Gln Trp Ala Val Gly His Leu Met
 1 5 10

<210> ~~SEQ ID NO: 5~~
 <211> ~~LENGTH: 8~~
 <212> ~~TYPE: PRT~~
 <213> ~~ORGANISM: Synthetic~~ → <2207>
 <221> MOD_RES
 <222> (1) ~~... (0)~~ delete
 <400> ~~SEQ ID NO: 5~~
 Asp Tyr Met Gly Trp Met Asp Phe
 1 5

<210> ~~SEQ ID NO: 6~~
 <211> ~~LENGTH: 8~~
 <212> ~~TYPE: PRT~~
 <213> ~~ORGANISM: Synthetic~~ → <2207>
 <221> MOD_RES
 <222> (1) ~~... (0)~~ delete
 <400> ~~SEQ ID NO: 6~~
 Asp Tyr ~~Nle~~ Gly Trp ~~Nle~~ Asp Phe
 1 5

"Nle" is invalid for use in the sequence.
 Use Xaa and explain
 in <2207>-<2237>
 section

<210> ~~SEQ ID NO: 7~~
 <211> ~~LENGTH: 8~~
 <212> ~~TYPE: PRT~~
 <213> ~~ORGANISM: Synthetic~~ → <2207>
 <221> MOD_RES
 <222> (1) ~~... (0)~~ delete

Xaa
 <2237><228> Xff = D-Asp
 <400> SEQ ID NO: 7
 Xff Tyr Nle Gly Trp Nle Asn Phe
 1 invalid .5 invalid

<210> SEQ ID NO: 8
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Synthetic

<2237><229> Xaa Xgg = D-Lys
 <2207>
 <2217> mod-RES
 <2227> (1)

<400> SEQ ID NO: 8
 Xgg Pro Arg Arg Pro Tyr Ile Leu
 1 5

1) Please consult Sequence Rules
for valid format.

2) Consult sample Sequence Listing
 (attached) for valid format

<110> Smith, John; Smithgene Inc.
 <120> Example of a Sequence Listing
 <130> 01-00001
 <140> PCT/EP98/00001
 <141> 1998-12-31
 <150> US 08/999,999
 <151> 1997-10-15
 <160> <
 <170> PatentIn version 2.0
 <210> 1
 <211> 389
 <212> DNA
 <213> Paramecium sp.
 <220>
 <221> CDS
 <222> (279)...(389)
 <300>
 <301> Doe, Richard
 <302> Isolation and Characterization of a Gene Encoding a
 Protease from Paramecium sp.
 <303> Journal of Genes
 <304> 1
 <305> 4
 <306> 1-7
 <307> 1988-06-31
 <308> 123456
 <309> 1988-06-31
 <400> 1
 agctgtagtc attcctgtgt cctcttctct ctgggcttct caccctgcta atcagatctc 60
 agggagagtg tcttgacctt cctctgctct tgcagcttca caggcaggca ggcaggcagc 120
 tgaatgtggca attgtctggca gtgccacagg ccttctagcc aggccttaggg tgggttccgc 180
 cgcggcgcgg cggccctctt cgcgctctct tcgcgctctt ctctcgtctt cctctcgtct 240

Consult this

Appendix 3, page 2

ggacctgatt aggtgagcag gaggagggggg cagtttagc atg gtt tca atg ttc agc 296
Met Val Ser Met Phe Ser

ttg tct ttc aaa tgg cct gga ttt tgt ttg ttt gtt tgt ttc ttc caa 300
Leu Ser Phe Lys Trp Pro Gly Phe Cys Leu Phe Val Cys Leu Phe Cln

tgt ccc aaa gtc ttc ccc tgt cac tca tca ttg cag ccg aat ctt 389
Cys Pro Lys Val Leu Pro Cys His Ser Ser Leu Gln Pro Asn Leu

<210> 2
<211> 37
<212> PRT
<213> Paramecium sp.

<400> 2
Met Val Ser Met Phe Ser Leu Ser Phe Lys Trp Pro Gly Phe Cys Leu
1 5 10

Phe Val Cys Leu Phe Cln Cys Pro Lys Val Leu Pro Cys His Ser Ser
20 25 30

Leu Gln Pro Asn Leu
35

<210> 3
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> Designed peptide based on size and polarity to act as a linker between the alpha and beta chains of Protein XYZ.

<400> 3
Met Val Asn Leu Glu Pro Met His Thr Glu Ile
1 5 10

<210> 4
<400> 4
000

[Annex VIII follows]

identifiers and their accompanying information as shown in the following table. The numeric identifier shall be used only in the "Sequence Listing." The order and presentation of the items of information in the "Sequence Listing" shall conform to the arrangement given below. Each item of information shall begin on a new line and shall begin with the numeric identifier enclosed in angle brackets as shown. The submission of those items of information designated with an "M" is mandatory. The submission of those items of information designated with an "O" is optional. Numeric identifiers <110> through <170> shall only be set forth at the beginning of the "Sequence Listing." The following table illustrates the numeric identifiers.

Numeric Identifier	Definition	Comments and Format	Mandatory (M) or Optional (O)
<110>	Applicant	Preferably max. of 10 names; one name per line; preferable format: Surname, Other Names and/or Initials	M
<120>	Title of Invention		M
<130>	File Reference	Personal file reference	M, when filed prior to assignment of appl. number
<140>	Current Application Number	Specify as: US 07/999,999 or PCT/US96/99999	M, if available
<141>	Current Filing Date	Specify as: yyyy-mm-dd	M, if available
<150>	Prior Application Number	Specify as: US 07/999,999 or PCT/US96/99999	M, if applicable include priority documents under 35 USC 119 and 120
<151>	Prior Application Filing Date	Specify as: yyyy-mm-dd	M, if applicable
<160>	Number of SEQ ID NOs	Count includes total number of SEQ ID NOs	M
<170>	Software	Name of software used to create the Sequence Listing	O
<210>	SEQ ID NO: #	Response shall be an integer representing the SEQ ID NO shown	M
<211>	Length	Respond with an integer expressing the number of bases or amino acid residues	M

<212>	Type	Whether presented sequence molecule is DNA, RNA, or PRT (protein). If a nucleotide sequence contains both DNA and RNA fragments, the type shall be "DNA." In addition, the combined DNA/RNA molecule shall be further described in the <220> to <223> feature section.	M
<213>	Organism	Scientific name, i.e. Genus/species, Unknown or Artificial Sequence. In addition, the "Unknown" or "Artificial Sequence" organisms shall be further described in the <220> to <223> feature section.	M
<220>	Feature	Leave blank after <220>. <221-223> provide for a description of points of biological significance in the sequence.	M, under the following conditions: if "n," "Xaa," or a modified or unusual L-amino acid or modified base was used in a sequence; if ORGANISM is "Artificial Sequence" or "Unknown"; if molecule is combined DNA/RNA.
<221>	Name/Key	Provide appropriate identifier for feature, preferably from WIPO Standard ST.25 (1998), Appendix 2, Tables 5 and 6	M, under the following conditions: if "n," "Xaa," or a modified or unusual L-amino acid or modified base was used in a sequence
<222>	Location	Specify location within sequence; where appropriate state number of first and last bases/amino acids	M, under the following conditions: if "n," "Xaa," or a modified or unusual L-amino acid or modified

in feature

base was used in
a sequence

<223>

Other Information

Other relevant
information;
four lines maximum

M, under the following conditions:
if "n," "Xaa," or
a modified or unusual L-amino acid
or modified base
was used in a
sequence; if
ORGANISM
is "Artificial
Sequence" or
"Unknown"; if
molecule is combined DNA/RNA.

<300>

Publication
Information

Leave blank
after <300>

0

<301>

Authors

Preferably max
of ten named
authors of publication; specify
one name per line;
preferable format:
Surname, Other
Names and/or
Initials

0

<302>

Title

0

<303>

Journal

0

<304>

Volume

0

<305>

Issue

0

<306>

Pages

0

<307>

Date

Journal date on which
data published;
specify as yyyy-mm-
dd, 1001-yyyy or
Season-yyyy

0

<308>

Database
Accession
Number

Accession number
assigned by database including
database name

0

<309>

Database Entry
Date

Date of entry in
database; specify
as yyyy-mm-dd or
1001-yyyy

0

<310>

Patent Document
Number

Document number;
for patent-type
citations only.
Specify as, for
example, US
07/999,999

0

<311>	Patent Filing Date	Document filing date, for patent-type citations only; specify as yyyy-mm-dd	0
<312>	Publication Date	Document publication date, for patent-type citations only; specify as yyyy-mm-dd	0
<313>	Relevant Residues	FROM (position) TO (position)	0
<400>	Sequence	SEQ ID NO should follow the numeric identifier and should appear on the line preceding the actual sequence	M

5. Section 1.024 is revised to read as follows:

1.024 Form and format for nucleotide and/or amino acid sequence submissions in computer readable form.

(a) The computer readable form required by 1.021(c) shall meet the following specifications:

- (1) The computer readable form shall contain a single "Sequence Listing" as either a diskette, series of diskettes, or other permissible media outlined in paragraph (c) of this section.
- (2) The "Sequence Listing" in paragraph (a) (1) of this section shall be submitted in American Standard Code for Information Interchange (ASCII) text. No other formats shall be allowed.
- (3) The computer readable form may be created by any means, such as word processors, nucleotide/amino acid sequence editors or other custom computer programs; however, it shall conform to all specifications detailed in this section.
- (4) File compression is acceptable when using diskette media, so long as the compressed file is in a self-extracting format that will decompress on one of the systems described in paragraph (b) of this section.
- (5) Page numbering shall not appear within the computer readable form version of the "Sequence Listing" file.
- (6) All computer readable forms shall have a label permanently affixed thereto on which has been hand-printed or typed: the name of the applicant, the title of the invention, the date on which the data were recorded on the computer readable form, the operating system used, a reference number, and an application serial number and filing date, if known.

(b) Computer readable form submissions must meet these format requirements:

- (1) Computer: IBM PC/XT/AT, or compatibles, or Apple Macintosh;
- (2) Operating System: MS-DOS, Unix or Macintosh;